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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,354	11/25/2003	Patrick L. Iversen	50450-8311.US03	8250
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King & Spalding LLP P.O. Box 889 Belmont, CA 94002-0889			EXAMINER EPFS SMITH, JANET L	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 04/27/2009	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/723,354

**Applicant(s)**

IVERSEN, PATRICK L.

**Examiner**

Janet L. Epps-Smith

**Art Unit**

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 31-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SE/US)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-24-09 has been entered.

### ***Priority***

2. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

3. The disclosure of the prior-filed application, Application No. 08/802859, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, the disclosure of 08/802859, filed 02/19/1997 fails to disclose support for the morpholino modified antisense oligomers recited in the methods of the instantly claimed invention. However, support is found in parent application 09/574570, filed 05/17/2000, thus Applicants are granted priority to 09/574570.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. Claims 31-47 are presently pending in the instant application.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 31-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Melvin et al. (WO97/12246) or Housman et al. (US Patent No. 6200754) in view of Arora et al. (2000) and Baker et al. (1999).

8. Melvin et al. teach the following:

See Summary pages 4-5, last paragraph of Summary:

9. Because the expression of CYP1B1 is very common in tumours of many different types, it is likely that this enzyme performs an essential function for the tumor cells, for example by inactivating endogenous anti-tumor compounds such as 2-methoxyestradiol. Consequently, another aspect of the invention is the reduction of CYP1B1 levels in tumor cells, for example by the use of suicide inhibitors or by using antisense RNA methods to decrease the synthesis of the protein.
10. Page 23 of Melvin et al. discloses the following:

**25. A substance for use in the reduction of CYP1B1 levels in tumour cells, said substance comprising a suicide inhibitor or means for producing antisense RNA to decrease the synthesis of CYP1B1.**

11. Melvin et al. does not teach wherein the antisense oligonucleotide is morpholino modified.

12. Housman et al. teach a method for producing an inhibitor of a conditionally essential gene, wherein in one embodiment the gene of interest is a cytochrome p450 gene selected from a group including CYP1A1, CYP1A2, CYP2A6, CYP2A7, CYP2B6, CYP2B7, CYP2C8, CYP2C9, CYP2C17, CYP2C18, CYP2C19, CYP2D6, CYP2E1, CYP2F1, CYP3A3, CYP3A4, CYP3A5, CYP3A7, CYP4B1, CYP7, CYP11, CYP17, CYP19, CYP21, and CYP27. Housman et al. further teach wherein the inhibitor is an antisense oligonucleotide. (see col. 73-76)

13. Housman et al. further teach wherein the inhibitors are designed to target intron regions of genes. In preferred embodiments the inhibitor or potential inhibitor is an oligonucleotide, e.g. an antisense oligonucleotide, preferably at least partially an oligodeoxyribonucleotide. The antisense oligonucleotide is complementary to a sequence which includes a sequence variance site. Usually, though not necessarily, the antisense oligonucleotide is perfectly complementary to a sequence of the target allelic form which includes a sequence variance site. The antisense oligonucleotide preferably is at least twelve nucleotides, more preferably at least seventeen nucleotides in length. In some cases the antisense oligonucleotide may advantageously be longer, for example, at least 20, 25, or 30 nucleotides in length. Also in preferred

embodiments, the oligonucleotide is no longer than 20, 25, 30, 35, 40, or 50 nucleotides. The optimal length will depend on a number of factors, which may include the differences in binding free energy of the oligonucleotide to the target sequence as compared to binding to the non-target allelic form, i.e., the non-target sequence variant, or the kinetics of nucleic acid hybridization. The oligonucleotide preferably contains at least one nucleic acid analog or modified linkage. Such complementary oligonucleotides may function in various ways, and those skilled in the art will know how to design the oligonucleotide accordingly. (col. 15-16)

14. Arora et al. teach the following, see Introduction:

"The present study uses phosphorodiamidate morpholino oligomers (PMOs) that represent a novel DNA chemistry with a six-membered morpholine ring instead of a deoxyribose sugar and the charged phosphodiester internucleoside linkage replaced by an uncharged phosphorodiamidate linkage (Summerton and Weller, 1997a). The lack of internucleoside charge allows PMOs to avoid nonspecific effects observed with the more commonly used phosphorothioate analogs that bind to cellular and extracellular proteins. Furthermore, PMOs are highly resistant to various nucleases and proteases (Hudziak et al., 1996) and extremely efficient inhibitors of translation via a nonRNase H, sequence-specific steric blockade process (Giles et al., 1998, 1999)."

15. Baker et al. teach the design of antisense oligonucleotides comprising morpholino sugar modifications, wherein the antisense oligonucleotides were designed to effectively interfere with translation initiation of a target transcript. In one embodiment, the antisense oligonucleotides were designed to target the AUG region of a target transcript. Baker et al. also taught wherein oligonucleotide comprised 19, 20, 22, or 24 nucleobases in length, see § 3.5.1.2, page 12. Additionally, Baker et al.

taught that antisense oligonucleotides can be used to target intron-exon borders in pre-mRNA to affect gene expression by modulating RNA splicing of a given gene target, See pages 8-9.

16. It would have been obvious to the ordinary skilled artisan to modify the antisense oligonucleotides targeting CY1B1 of Melvin et al. and the antisense targeting CY3A4 and other cytochrome p450 genes described in Housman et al. with the morpholino modifications of Arora et al. and Baker et al. The ordinary skilled artisan would have been motivated to modify the teachings of Melvin et al. and Housman et al. to design antisense oligonucleotides targeting C1YP1B1 and CYP3A4 since Melvin et al. and Housman et al. clearly provides this motivation, and further to modify these oligonucleotides to target the initiation codon and sequences which regulate RNA splicing, comprise at least 15 nucleotides in length and further comprise morpholino modifications since the prior art clearly teach that antisense oligonucleotide comprising the morpholino modification are superior to unmodified oligonucleotides and are effective inhibitors of translation of target mRNA transcripts.

17. Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

***Response to Amendment/Arguments***

18. The rejection of claims 40-47 under 35 USC 112, 2<sup>nd</sup> ¶ is withdrawn in response to Applicant's amendment.
19. The rejection of claims 31-47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn.
20. The rejection of claims 31-47 under 35 U.S.C. 112, first paragraph, because the specification, for lack of enablement is withdrawn in response to Applicant's amendment to claims.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Weitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/  
Primary Examiner, Art Unit 1633